SCIENTIFIC ABSTRACT OF PROTOCOL

This protocol is a study of patients with recurrent malignant gliomas who have failed standard therapy. In an attempt to increase the patient's immune response to the tumor, dendritic cells (DC) cultured from patients' peripheral blood mononuclear cells (PBMC) obtained by leukapheresis will be loaded with apoptotic autologous glioma cells obtained during clinically indicated tumor resection. To increase the efficacy of the intradermal vaccination with the dendritic cells, the patients' skin-derived fibroblasts will be transfected with the retroviral vector encoding interleukin-4 (IL-4) gene and co-administered with DC intradermally at the patients' thigh. Because DCs are potent professional antigen presenting cells (APCs) capable of presenting antigen (Ag) for T cell activation, it is expected that the vaccination will induce anti-glioma immunity in the patients' systemic immune systems. Preclinical studies suggest that local continuous expression of IL-4 at the vaccine will enhance the induction of immunity by facilitating migration of DC from the vaccine sites to the lymphoid organs. This enhancement appears to be mediated through activation of endothelial cells. Vaccinations will be repeated twice with a two-week interval. Animal models have shown the advantage of this combined strategy (DC plus IL-4 fibroblasts) over DC alone.

We have the following specific objectives:

1. To assess the local and systemic toxicity associated with this form of vaccine.
2. To evaluate the local immune response engendered by this form of vaccine.
3. To evaluate the ability of this vaccine design to induce cytotoxic T-lymphocytes capable of lysing autologous glioma cells *in vitro*.
4. To evaluate the ability of this vaccine design to induce humoral immune response to glioma specific antigens.
5. To evaluate preliminary clinical activity of this vaccine.